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### Remarks

#### Claim amendments

Claims 1-47 are cancelled, and claims 48-83 are new (support is from original claims 1-34 and from throughout the specification). All new claims reflect changes in plurality of words (molecule vs. molecules; ligand vs. ligands), or particular terms (determining a quantity of vs. obtaining a measure of), added to provide proper antecedent bases for the terms in dependent claims, and to clarify. For example, new claim 48 is based on original claim 1 but written to delete "one or more target molecules" and insert "a target molecule" since both versions allow one or more target molecules, but the new version provides proper antecedent basis for later dependent claims referring to "the target molecule." Moreover, new claims 52, 53, 55, 57, 72 and 73 (prior claims 5, 6, 8, 10, 25 and 26) have corrected the grammar from "molecules include" to "molecule includes."

New claims 56 and 59 (prior 9 and 12) contain amended Markush language to properly recite "the group consisting of" rather than "*a* group consisting of." New claim 62 (prior 15) is written to read "first sample" to properly depend from claim 48. New claims 68, 70, 76, 77 and 78 (prior claims 21, 23, 29, 30 and 31) are written to correct "obtaining a measure" or "determining a concentration" to correlate to the language set forth in claim 48 – namely, "determining a quantity."

All of the above amendments represent amendments to clarify, correct grammar, and provide proper, consistent antecedent bases for all terms in dependent claims. No new matter is added with these amendments.

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New claims 75 and 79 (prior 28 and 32), originally multiple-dependent from original claims 24-27, and new claims 77 or 78 (prior 30 or 31), respectively, are written to (a) remove the dependency from claim 73 (prior 26) for new claim 75 (prior 28) and add a new dependent claim which depends only from claim 73 (prior 26) for new claim 82 (prior 46); or (b) to remove the dependency from new claim 78 (prior 31) for new claim 79 (prior 32) and add a new dependent claim which depends only from new claim 78 (claim 83). These changes are strictly changes in form, to separate out dependent claims that cannot be properly claimed using the antecedents contained in the multiple-dependent claims, as originally written. No new matter is added with these changes and new claims.

New claim 78 is written to delete the phrase “or to multiple substrates wherein each substrate is contained in a separate chamber” because this phrase is redundant with the immediately preceding phrase “an immobilized ligand wherein the ligand is immobilized by attachment to a substrate in a single chamber” (now changed to “an a plurality of immobilized ligand ligands wherein the each ligand is immobilized by attachment to a substrate in a single chamber” to properly recite antecedents in claim 48). As originally written, an immobilized ligand attached to a substrate in a single chamber is no different from an immobilized ligand attached to multiple substrates, each substrate contained in a separate chamber. The effect is the same – a single chamber with a ligand immobilized to a substrate. Support for this deletion amendment, and the amendment to a “plurality of ... ligands, each ... immobilized to...” is found in Figs. 3 and 4, and the text accompanying Figs. 3 and 4, which is Examples G and H, pp. 18-22. Applicants respectfully submit that no new matter is added with this new claim language.

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Objections to Claims and Rejections based on 35 U.S.C. § 112, para. 2 – Indefiniteness

With the above-described new claims and changes to the language therein with respect to the original claims, and cancellation of claims 1-47, Applicants respectfully submit that all claim objections and claim rejections based on indefiniteness have been addressed. Applicants respectfully request withdrawal of the claim objections and rejections for indefiniteness based on 35 U.S.C. § 112, para. 2.

Prior art rejections under 35. U.S.C. § 103 (a)

The core rejection of new claims 48-49, 52-55, 60-71, and 70 (prior claims 1-2, 5-8, 13-24 and 33) as being unpatentable over Dodge et al. (US2002/0051974) in view of Freytag et al. (*Clin. Chem.* 30, 417-420, 1984 – hereinafter “Freytag 1”) for reasons of obviousness, fails because of two important distinctions. First, Dodge discloses that a) a capture molecule initially binds to the target molecule in the sample to form a capture molecule-target molecule complex, and then b) a detector molecule binds to the target molecule-capture molecule complex. As seen in claim 48 of the instant application, embodiments of the presently claimed invention require adding only “a preparation of a nucleic acid aptamer specific for each the target molecule” to the sample; then “allowing substantially all of the target molecules molecule in the first sample to bind with the aptamer” to form an aptamer-target molecule complex; and then “separating unbound aptamer from the first sample” by contacting the aptamer-target molecule complex so formed “with immobilized ligand, thereby binding the ligand to unbound aptamer, so as to recover a second sample of aptamer bound to target molecule;” and finally “using a

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quantitative replicative ... to determine a quantity of aptamer specific for the target molecule ....” Absolutely nowhere is there a requirement for a capture molecule-target molecule complex before binding an aptamer.

Second, although Dodge discloses that the detector molecule can be any aptamer (DNA oligonucleotide), Dodge specifically shows in Fig. 1A that the probe has a fluorescent reporter dye/quencher pair such that the reporter only fluoresces upon incorporation of the probe into amplified PCR product; Dodge specifically states in para. [0068] that “the probe preferably has a 5’ reporter dye and a downstream 3’-quencher dye covalently bonded to the probe which allows fluorescent resonance energy transfer; and Dodge discloses examples of the aptamer detector molecule (Example 1) as using only oligonucleotide probes have reporter dye/quencher pairs (5’-FAM...TAMRA-3’) – see para. [0105], [0108], [0111].

There is no motivation to combine the references of Dodge and Freytag 1, and no suggestion in either reference to modify Dodge to incorporate the methodologies of Freytag, or eliminate the need for a capture molecule-target molecule-detector molecule ternary complex to that of the presently claimed binary complex of only aptamer bound to target molecule.

Without the primary rejection based on Dodge and Freytag 1, no other obviousness rejection based on additional references combined with the core Dodge and Freytag 1 combination hold water. Applicants also respectfully submit that the present references add nothing to those which have been cited in previous office actions and rebutted in previous responses.

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Applicants respectfully submit that all claims are in condition for allowance and therefore request withdrawal of all rejections under 35 USC § 103(a) for reasons of obviousness.

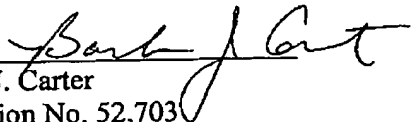
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### Conclusion

It is believed that no extension of time is required or that any fees are needed for submission of this communication; however, if fees are required for the timely consideration of this application, please charge deposit account number 19-4972.

It is submitted that all claim objections and rejections have been addressed, and that all of the pending claims are now in a condition for allowance. Accordingly, Applicants respectfully request reconsideration of the application and issuance of a notice of allowance. The Examiner is requested to telephone the undersigned if any matters remain outstanding so that they may be resolved expeditiously.

Respectfully submitted,

  
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